IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re U.S. PATENT NUMBER 6,893,636 Issued: May 17, 2005

Inventor(s): Mitchell REFF et al. Confirmation No.: 2038

Application No. 09/019,441 Group Art Unit: 1644

Filed: February 5, 1998 Examiner: Phuong N. HUYNH

Title: GAMMA-1 ANTI-HUMAN CD23 MONOCLONAL ANTIBODIES AND USE THEREOF AS THERAPEUTICS

* * * * *

REQUEST FOR CERTIFICATE OF CORRECTION

PURSUANT TO 37 C.F.R. § 1.323

ATTN: Certificate of Correction Branch
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

Pursuant to 37 C.F.R. §1.323, the patentees respectfully request that a Certificate of Correction be issued for the above-identified patent to correct a typographical errors in the specification and in claim 13.

Applicants request that the term "6G5" be replaced with the term "5E8" at column 27, line 64. The term "6G5" is clearly incorrect, as evident from the disclosure of the 5E8 heavy chain variable region beginning at column 28 and from reference to SEQ ID NOs: 7 and 8, which set forth the nucleotide and amino acid sequences, respectively, of the 5E8 heavy chain variable region.

Applicants further request that claim 13 be amended to depend from claim 7. On 28 April 2004, the applicants submitted an amended version of the claims that ultimately issued in the above-identified patent (copy enclosed). On 7 July 2004, the examiner renumbered the claims in conjunction with a Notice of Allowance (Paper No. 06282004, copy enclosed). The applicants point out that claim 54 in the 28 April 2004 submission was renumbered as claim 13 by the examiner. Claim 54 is dependent upon claim 48, and claim 48 was renumbered as

claim 7 prior to issuance. Accordingly, issued claim 13 should depend from issued claim 7, not claim 8. This error is also apparent from the fact that claims 13 and 14 have the same identical text (copy enclosed).

The proposed corrections are both typographical in nature, and therefore, the request for correction does not introduce new matter or require reexamination. The typographical error in the specification is the fault of the applicant, but the error in claim 13 is the fault of the Patent Office. The required fee under 37 C.F.R. §1.20(a) is submitted herewith via EFS Web charge authorization.

Respectfully submitted,
PILLSBURY WINTHROP SHAW PITTMAN LLP

/ julie broadus meigs /

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PTO/SB/44 (MODIFIED)

UNITED STATES PATENT AND TRADEMARK OFFICE
CERTIFICATE OF CORRECTION

PATENT NO. : 6,893,636

APPLICATION NO.: 09/019,441

ISSUE DATE. : May 17, 2005

INVENTOR(S) : Mitchell E. REFF et al.

It is certified that an error appears or errors appear in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

Col. 27, line 64
replace "6G5"
with --5E8--.

Claim 13
replace "8"
with --7--.

MAILING ADDRESS OF SENDER (Please do not use customer number below):

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1644

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re PATENT APPLICATION OF

Mitchell R. REFF et al. Group Art Unit: 1644

Application Serial No. 09/019,441 Examiner: Phuong N. Huynh

Filed: February 5, 1998

Title: GAMMA-1 AND GAMMA-3 ANTI-HUMAN CD23 MONOCLONAL ANTIBODIES AND USE THEREOF AS THERAPEUTICS

* * * * *

AMENDMENT PURSUANT TO 37 C.F.R. § 1.111

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

This is in response to the official action dated January 16, 2004, wherein the claims were rejected under 35 U.S.C. § 112, second paragraph. The applicants traverse the outstanding rejections in view of the following amendments and remarks. This response is timely filed with the enclosed petition for a one-month extension of time and payment of the requisite fee.

Amendments To The Specification

Please amend the paragraph beginning at page 43, line 23, as follows:

A second independent PCR amplification of the light chain from cDNA of primate monoclonal antibody 6G5 was effected using a 5' primer early leader sequence of lambda light chain family 2 (primer 745) (SEQ ID NO: 15) and the 3' J region primer 926 (SEQ ID NO: 17). (See Primers for PCR of the lambda light chain variable domain of 6G5 in Tables 1-3 (SEQ ID NOs: 9-25). The isolated PCR product (see technique above) was cloned into TA vector by using the Original TA Cloning(Kit (Invitrogen Catalog # K2000-01). The isolated miniprep DNA (see technique above) was examined under agarose gel electrophoresis after digestion with EcoR I restriction endonuclease. The resultant PCR product comprised in the TA vector was then sequenced (as described previously) using Sp6 (SEQ ID NO: 26) and M13(-40) (SEQ ID NO: 27) forward primers (See Sequencing primers in Table 4 (SEQ ID NOs: 26-35)). The resultant light chain sequence was identical to that of light chain from the first PCR. This entire sequence of the light chain variable domain of primate monoclonal anti-human CD23 antibody 6G5 is presented below ~~(SEQ ID NO: 1)~~ as an alignment of the nucleotide sequence (SEQ ID NO:1) and the encoded amino acid sequence (SEQ ID NO:2).

Please amend the captioned section beginning at page 44, line 8, as follows:

Light chain variable region of primate monoclonal antibody

anti-human CD23 6G5 Leader

```
Met Ala Trp Thr Leu Leu Leu Val Thr Leu Leu Thr Gln Gly Thr
ATG GCC TGG ACT CTG CTC CTC GTC ACC CTC CTC ACT CAG GGC ACA
             -1
Gly Ser Trp Ala
GGA TCC TGG GCT
```

(SEQ ID NO: 1 – bases 1-57)

Please amend the captioned section beginning at page 44, line 15, as follows:

Mature Protein (Numbering is Kabat)

Framework 1

```
 1                                   9  11
Gln Ser Ala Pro Thr Gln Pro Pro Ser Val Ser Gly Ser Pro Gly
CAG TCT GCC CCG ACT CAG CCT CCC TCT GTG TCT GGG TCT CCT GGA
```

```
             20          23
Gln Ser Val Thr Ile Ser Cys
CAG TCG GTC ACC ATC TCC TGC
```
(SEQ ID NO: 1 – bases 58-123)

Please amend the captioned section beginning at page 44, line 23, as follows:

CDR 1

```
 24          27 27A 27B 27C  28                      34
Thr Gly Thr Ser Asp Asp Val Gly Gly Tyr Asn Tyr Val Ser
ACT GGA ACC AGC GAT GAC GTT GGT GGT TAT AAC TAT GTC TCC
```
(SEQ ID NO: 1 – bases 124-165)

Please amend the captioned section beginning at page 44, line 27, as follows:

Framework 2

```
 35                  40                                  49
Trp Tyr Gln His His Pro Gly Lys Ala Pro Lys Leu Met Ile Tyr
TGG TAC CAA CAC CAC CCA GGC AAA GCC CCC AAA CTC ATG ATT TAT
```
(SEQ ID NO: 1 – bases 166-210)

Please amend the captioned section beginning at page 45, line 1, as follows:

CDR2

```
50                      56
Asp Val Ala Lys Arg Ala Ser
GAT GTC GCT AAG CGG GCC TCA
```
(SEQ ID NO: 1 – bases 211-231)

Please amend the captioned section beginning at page 45, line 5, as follows:

Framework 3

```
 57          60                                  70
Gly Val Ser Asp Arg Phe Ser Gly Ser Lys Ser Gly Asn Thr Ala
GGG GTC TCT GAT CGC TTC TCT GGC TCC AAG TCT GGC AAC ACG GCC
                                    80
Ser Leu Thr Ile Ser Gly Leu Gln Ala Glu Asp Glu Ala Asp Tyr
TCC CTG ACC ATC TCT GGG CTC CAG GCT GAG GAC GAG GCT GAT TAT

     88
Tyr Cys
TAC TGT
```
(SEQ ID NO: 1 – bases 232-327)

Please amend the captioned section beginning at page 45, line 15, as follows:

CDR 3

```
 89  90                  95 95A  96  97
Cys Ser Tyr Thr Thr Ser Ser Thr Leu Leu
TGT TCA TAT ACA ACC AGT AGC ACT TTG TTA
```

(SEQ ID NO: 1 – bases 328-357)

Please amend the captioned section beginning at page 45, line 19, as follows:

Framework 4

```
 98     100                      106 106A 107
Phe Gly Arg Gly Thr Arg Leu Thr Val Leu Gly
TTC GGA AGA GGG ACC CGG TTG ACC GTC CTA GGT
```

(SEQ ID NO: 1 – bases 358-390)

Please amend the captioned section beginning at page 45, line 23, as follows:

2) Cloning the heavy chain variable domain of primate monoclonal anti-human CD23 antibody 6G5 by PCR

The first PCR amplification of the heavy chain variable domain from cDNA of primate monoclonal antibody 6G5 was performer by using the set of early leader sequence primers described supra and the 3' J region primer GE244 (SEQ ID NO: 23). These primers are in Tables 1-3 (SEQ ID NOs: 9-25) infra. This reaction resulted in a 350 base PCR product. This 350 base product (purified as described supra), was digested with Nhe I and Sal I, and ligated into N5LG1 and digested with the same endonucleases in the first PCR amplification. The resultant ligation mixture was transformed into host cells using the same techniques for cloning the light chain. Plasmid N5LG1 containing the 350 base PCR product was then isolated and sequenced (using sequencing primers 266 (SEQ ID NO: 32) and 268) (SEQ ID NO: 33). (These Sequencing primers are set forth in Table 4 (SEQ ID NOs: 26-35).)

Please amend the paragraph beginning at page 46, line 15, as follows:

A second independent PCR reaction was conducted to amplify and isolate the heavy chain variable domain of primate monoclonal antibody 6G5 using a 5' early leader sequence primer for family 1 (MB1503) (SEQ ID NO: 18) and a 3' J' region primer GE244 (SEQ ID NO: 23). (These primers are also contained in Tables 1-3 (SEQ ID NOs: 9-25)) The resultant

PCR product was then cloned into the NSLG1 using the same techniques described supra. Its sequence was found to be identical to the first PCR product.

Please amend the paragraph beginning at page 46, line 24, as follows:

Therefore, in order to clone the whole heavy variable domain of 6G5 including the missing 5' terminus a new longer 3' primer (MB1533) (SEQ ID NO: 25) which included the CDR3 and framework 4 regions of the 6G5 heavy variable chain was then used in a third independent PCR reaction with the family 1 5' primer (MB1503) (SEQ ID NO: 18). (These primers are also contained in Tables 1-3 (SEQ ID NOs: 9-25).)

Please amend the captioned section beginning at page 47, line 6, as follows:

A fourth independent PCR was performed using the same primers as the third PCR amplification. This resulted in a PCR product which was isolated and cloned into the TA vector as described previously. The sequence of the fourth independent PCR product was found to be identical to that obtained in the third PCR amplification. This sequence, which comprises the heavy chain variable domain of primate monoclonal anti-human CD23 antibody 6G5, is presented below ~~(SEQ ID NO.: 2)~~ as an alignment of the nucleotide sequence (SEQ ID NO: 3) and the encoded amino acid sequence (SEQ ID NO:4).

Please amend the captioned section beginning at page 47, line 15, as follows:

Heavy chain variable region of primate monoclonal

antibody anti-human CD23 6G5

Leader

```
Met Lys His Leu Trp Phe Phe Leu Leu Leu Val Ala Ala Pro Arg
ATG AAA CAC CTG TGG TTC TTC CTC CTC CTG GTG GCA GCT CCC AGA
             -1
Trp Val Leu Ser
TGG GTC CTG TCC
```

(SEQ ID NO: 3 – bases 1-57) -

Please amend the captioned section beginning at page 47, line 23, as follows:

Mature Protein (Numbering is Kabat)

Framework 1

```
 1                                  10
Gln Leu Gln Leu Gln Glu Ser Gly Pro Gly Val Val Lys Pro Ser
CAG CTG CAG CTG CAG GAG TCG GGC CCA GGA GTG GTG AAG CCT TCG
            20                                          30
Glu Thr Leu Ser Leu Thr Cys Ala Val Ser Gly Gly Ser Val Ser
GAG ACC CTG TCC CTC ACC TGC GCT GTC TCT GGT GGC TCT GTC AGC
```

(SEQ ID NO: 3 – bases 58-147)

Please amend the captioned section beginning at page 48, line 1, as follows:

CDR 1

```
 31              35 35a
Ser Ser Asn Trp Trp Thr
AGT AGT AAC TGG TGG ACC
```

(SEQ ID NO: 3 – bases 148-165)

Please amend the captioned section beginning at page 48, line 5, as follows:

Framework 2

```
36              40                                  49
Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile Gly
TGG ATC CGC CAG CCC CCA GGG AAG GGA CTG GAG TGG ATT GGA
```

(SEQ ID NO: 3 – bases 166-207)

Please amend the captioned section beginning at page 48, line 16, as follows:

CDR2

```
 50      52 52A  53                          60
Arg Ile Ser Gly Ser Gly Gly Ala Thr Asn Tyr Asn Pro Ser Leu
CGT ATC TCT GGT AGT GGT GGG GCC ACC AAC TAC AAC CCG TCC CTC
65
Lys Ser
AAG AGT
```

(SEQ ID NO: 3 – bases 208-258)

Please amend the captioned section beginning at page 48, line 16, as follows:

Framework 3

```
 66                  70                                      80
Arg Val Ile  Ile  Ser Gln Asp Thr Ser Lys Asn Gln Phe Ser Leu
CGA GTC ATC ATT TCA CAA GAC ACG TCC AAG AAC CAG TTC TCC CTG
```

```
     82 82a 82b 82c 83                                  90
Asn Leu Asn Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
AAC CTG AAC TCT GTG ACC GCC GCG GAC ACG GCC GTG TAT TAC TGT
     94
Ala Arg
GCC AGA
```

(SEQ ID NO: 3 – bases 259-354)

Please amend the captioned section beginning at page 48, line 26, as follows:

CDR 3

```
 95                  100 100a 100b 100c 100d 101 102
Asp Trp Ala Gln Ile Ala Gly  Thr  Thr  Leu  Gly Phe
GAT TGG GCC CAA ATA GCT GGA  ACA  ACG  CTA  GGC TTC
```

(SEQ ID NO: 3 – bases 355-390)

Please amend the captioned section beginning at page 49, line 1, as follows:

Framework 4

```
103                          110         113
Trp Gly Gln Gly Val Leu Val Thr Val Ser Ser
TGG GGC CAG GGA GTC CTG GTC ACC GTC TCC TCA
```

(SEQ ID NO: 3 – bases 391-423)

Please amend the captioned section beginning at page 50, line 3, as follows:

1. Cloning the light chain variable domain of primate monoclonal anti-human CD23 antibody 5E8 by PCR

The first PCR reaction of the light chain variable domain from FEE cDNA was carried out using a set of kappa early leader sequence primers and the 3' J region primer GE204 (SEQ ID NO: 13). (See primers for PCR of the kappa light chain variable domain of 5E8 in Tables 1-3 (SEQ ID NOs: 9-25)). A 420 base PCR product was obtained. The isolated 420 base PCR product was digested with Bgl II and BsiW I restriction endonucleases, cloned into the mammalian expression vector N5KG4P and sequenced using GE108 (SEQ ID NO: 29) and 377 (SEQ ID NO: 30) primers (which are contained in Table 4 (SEQ ID NOs: 26-35)): The mammalian expression vector N5KG4P is identical to the vector N5LG4P except it contains the human kappa light chain constrant region is place of the human lambda light

chain constant region. Sequencing of this 420 polynucleotide DNA revealed that it contains the entire kappa light chain variable domain.

Please amend the paragraph beginning at page 50, line 21, as follows:

A second independent PCR of the light chain variable region was performed using the 5' family 1 primer GE201 (SEQ ID NO: 9) and the 3' primer GE204 (SEQ ID NO: 13). (See primers for PCR of the kappa light chain variable domain of 5E8 in Tables 1-3 (SEQ ID NOs: 9-25)). The isolated PCR product was cloned into the TA vector (using methods previously described) and sequenced using Sp6 (SEQ ID NO: 26) and T7 promoter (SEQ ID NOs: 28) primers. Sequencing revealed that this PCR product was identical to that obtained from the first PCR. The entire sequence of the light chain variable domain of primate monoclonal anti-human CD23 antibody 5E8 is presented below ~~(SEQ ID NO: 3)~~ , as an alignment of the nucleotide sequence (SEQ ID NO: 5) and the encoded amino acid sequence (SEQ ID NO:6).

Please amend the captioned section beginning at page 51, line 1, as follows:

Light chain variable region of primate monoclonal antibody anti-human CD23 5E8

Leader

```
Met Asp Met Arg Val Pro Ala Gln Leu Leu Gly Leu Leu Leu Leu
ATG GAC ATG AGG GTC CCC GCT CAG CTC CTG GGG CTC CTT CTG CTC
                          -1
Trp Leu Pro Gly Ala Arg Cys
TGG CTC CCA GGT GCC AGA TGT
```

(SEQ ID NO: 5 – bases 1-66)

Please amend the captioned section beginning at page 51, line 9, as follows:

Mature Protein (Numbering is Kabat)

Framework 1

```
 1                                   10
Asp Ile  Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val
GAC ATC CAG ATG ACC CAG TCT CCA TCT TCC CTG TCT GCA TCT GTA
                 20         23
Gly Asp Arg Val Thr Ile Thr Cys
GGG GAC AGA GTC ACC ATC ACT TGC
```

(SEQ ID NO: 5 – bases 67-135)

Please amend the captioned section beginning at page 51, line 17, as follows:

CDR 1

```
 24                        30              34
Arg Ala Ser Gln Asp Ile  Arg Tyr Tyr Leu Asn
AGG GCA AGT CAG GAC ATT AGG TAT TAT TTA AAT
```

(SEQ ID NO: 5 – bases 136-168)

Please amend the captioned section beginning at page 51, line 21, as follows:

Framework 2

```
 35                  40                                  49
Try Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr
TGG TAT CAG CAG AAA CCA GGA AAA GCT CCT AAG CTC CTG ATC TAT
```

(SEQ ID NO: 5 – bases 169-213)

Please amend the captioned section beginning at page 51, line 25, as follows:

CDR2

```
50                      56
Val Ala Ser Ser Leu Gln Ser
GTT GCA TCC AGT TTG CAA AGT
```

(SEQ ID NO: 5 – bases 214-234)

Please amend the captioned section beginning at page 51, line 29, as follows:

Framework 3

```
 57          60                                      70
Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Glu Phe
GGG GTC CCA TCA AGG TTC AGC GGC AGT GGA TCT GGG ACA GAG TTC
                                  80
Thr Leu Thr Val Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr
ACT CTC ACC GTC AGC AGC CTG CAG CCT GAA GAT TTT GCG ACT TAT
     88
Tyr Cys
TAC TGT
```

(SEQ ID NO: 5 – bases 235-330)

Please amend the captioned section beginning at page 52, line 7, as follows:

CDR 3

```
89  90                              97
Leu Gln Val Tyr Ser Thr Pro Arg Thr
CTA CAG GTT TAT AGT ACC CCT CGG ACG (SEQ ID NO: 5 – bases 331-357)
```

Please amend the captioned section beginning at page 52, line 11, as follows:

Framework 4

```
98      100                             107
Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
TTC GGC CAA GGG ACC AAG GTG GAA ATC AAA (SEQ ID NO: 5 – bases 358-387)
```

Please amend the captioned section beginning at page 52, line 15, as follows:

2) Cloning the heavy chain variable domain of primate monoclonal anti-human CD23 antibody 5E8 by PCR

The first PCR of the heavy chain variable domain of 5E8 was performed using a set of 5' early leader heavy chain sequence primers and the 3' primer GE210 (SEQ ID NO: 24). (See primers for PCR of the heavy chain variable domain of 6G5 and 5E8 in Table 1 (SEQ ID NOs: 9-13)). A 420 base PCR product appeared in the family 3 primer reaction. The PCR product was purified and then digested with Nhe I and Sal I and cloned into the mammalian expression vector N5KG4P vector (as described previously). The PCR product was sequenced using the 268 (SEQ ID NO: 33) and 928 (SEQ ID NO: 35) primers. (See sequencing primers in Table 4 (SEQ ID NOs: 26-35).)

Please amend the paragraph beginning at page 52, line 28, as follows:

A second independent PCR of the heavy chain variable domain of 5E8 was performed using the family 3 5' primer GE207 (SEQ ID NO: 20) and the 3' primer GE210 (SEQ ID NO: 24). (See primers for PCR of the, heavy chain variable domain of 6G5 and 5E8 in Tables 1-3 (SEQ ID NOs: 9-25)). The isolated PCR product was cloned into a TA vector using the same techniques previously described and sequenced by using Sp6 (SEQ ID NO: 26) and T7 (SEQ ID NO: 28) primers. Sequencing revealed that the TAC at codon 91 had been changed into TGC.

Please amend the paragraph beginning at page 53, line 6, as follows:

In order to determine the appropriate codon at 91, a third independent PCR was performed using the same primers as the second PCR (see above). The PCR product was again cloned into a TA vector and sequenced using Sp6 (SEQ ID NO: 26) and T7 (SEQ ID NO: 28) primers. The sequence was found to be identical to the heavy chain variable sequence obtained in the first PCR. Therefore, the TGC at position 91 in the second independent PCR product is apparently the result of an error introduced during PCR. This entire sequence of the heavy chain variable domain of primate monoclonal anti-human CD23 antibody 6G5 is presented below ~~(SEW ID NO: 4)~~ , as an alignment of the nucleotide sequence (SEQ ID NO: 7) and the encoded amino acid sequence (SEQ ID NO:8).

Please amend the captioned section beginning at page 53, line 18, as follows:

Heavy chain variable region of primate monoclonal antibody

anti-human CD23 5E8 Leader

```
Met Glu Phe Gly Leu Ser Trp Val Phe Leu Val Pro Leu Leu Lys
ATG GAG TTT GGG CTG AGC TGG GTT TTC CTT GTT CCT CTT TTG AAA
             -1
Gly Val Gln Cys
GGT GTC CAG TGT
```

(SEQ ID NO: 7 - bases 1-57)

Please amend the captioned section beginning at page 53, line 26, as follows:

Mature Protein (Numbering is Kabat)

Framework 1

```
 1                                   10
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Ala Lys Pro Gly
GAG GTG CAG CTG GTG GAG TCT GGG GGC GGC TTG GCA AAG CCT GGG
                  20                                    30
Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Arg Phe Thr
GGG TCC CTG AGA CTC TCC TGC GCA GCC TCC GGG TTC AGG TTC ACC
```

(SEQ ID NO: 7 - bases 58-147)

Please amend the captioned section beginning at page 54, line 2, as follows:

CDR 1

```
 31                35 35a 35b
Phe Asn Asn Tyr Tyr Met Asp
TTC AAT AAC TAC TAC ATG GAC
```

(SEQ ID NO: 7 - bases 148-168)

Please amend the captioned section beginning at page 54, line 6, as follows:

Framework 2

```
 36                40                                        49
Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Val Ser
TGG GTC CGC CAC GCa CCA GGG CAG GGG CTG GAG TGG GTC TCA
```

(SEQ ID NO: 7 - bases 169-210)

Please amend the captioned section beginning at page 54, line 10, as follows:

CDR2

```
 50        52 52A  53                              60
Arg Ile  Ser Ser Ser Gly Asp Pro Thr Trp Tyr Ala Asp Ser Val
CGT ATT AGT AGT AGT GGT GAT CCC ACA TGG TAC GCA GAC TCC GTG
65
Lys Gly
AAG GGC
```

(SEQ ID NO: 7 - bases 211-261)

Please amend the captioned section beginning at page 54, line 17, as follows:

Framework 3

```
 66                70                                            80
Arg Phe Thr Ile Ser Arg Glu Asn Ala Asn Asn Thr Leu Phe Leu
AGA TTC ACC ATC TCC AGA GAG AAC GCC AAC AAC ACA CTG TTT CTT
     82 82a 82b 82c 83                            90
Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
CAA ATG AAC AGC CTG AGA GCT GAG GAC ACG GCT GTC TAT TAC TGT
94
Ala Ser
GCG AGC
```

(SEQ ID NO: 7 - bases 262-357)

Please amend the captioned section beginning at page 54, line 27, as follows:

CDR 3

```
 95                  100 101
Leu Thr Thr Gly Ser Asp Ser
TTG ACT ACA GGG TCT GAC TCC
```

(SEQ ID NO: 7- bases 358-378)

Please amend the captioned section beginning at page 55, line 1, as follows:

Framework 4

```
103                         110         113
Trp Gly Gln Gly Val Leu Val Thr Val Ser Ser
TGG GGC CAG GGA GTC CTG GTC ACC GTC TCC TCA
```

(SEQ ID NO: 7 - bases 379-411)

Please amend the paragraph beginning at page 56, line 3, as follows:

A first PCR was done using N5KG4P + 5E8 as a template and a 3' primer (corresponding to codon 71 to 79) and which contains a mutation at codon 75 (AAC changed to AAG, Primer MB1654 (SEQ ID NO: 39), and a 5' primer at the beginning of the leader sequence (Primer MB1650) (SEQ ID NO: 36). (See PCR Primers Used for the Generation of a Glycosylation Mutant of the Heavy Chain Variable Region 5E8 set forth in Table 5 (SEQ ID NOs: 36-39)).

Please amend the paragraph beginning at page 56, line 11, as follows:

A second PCR was performed on the same template by using a 5' primer (corresponding to codon 71 to 79) containing the same mutation (Primer MB1653) (SEQ ID NO: 38) and a 3' primer from the end of framework 4 (Primer MB1651) (SEQ ID NO: 37) (See PCR Primers Used for the Generation of a Glycosylation Mutant of the Heavy Chain Variable Region of 5E8 in Table 5 (SEQ ID NOs: 36-39).)

Please amend the paragraph beginning at page 56, line 18, as follows:

These two PCR products were isolated and mixed in equal molar ratios. A third independent PCR was then carried out by using the mixture of the first and second PCP products as a template with a 5' primer used in the first PCR (MB1650) (SEQ ID NO: 36) and a 3' primer used in the second PCR (MP 1651) (SEQ ID NO: 37) (See PCP Primers Used for

the Generation of a Glycosylation Mutant of the Heavy Chain Variable Region in Table 5 (SEQ ID NOs: 36-39).) The PCR product obtained in third PCR was found to contain the heavy variable domain coding region of 5E8 wherein the asparagine 75 had been changed to lysine.

Please amend Tables 1-5 beginning at page 57, line 8 (in their entirety), as follows:

Table 1

Primers for PCR of the kappa light chain variable domain of 5E8

NAME	Light chain Vk -early leader 5' (Bgl II)	FAMILY
	-22 -21 -20 -19 -18 17 -16 -15 -14	
GE201	5' AT CAC AGA TCT CTC ACC ATG GAC ATG AGG GTC CCC GCT CAG 3'	1
	~~(SEQ ID NO: 5)~~ (SEQ ID NO: 9)	
GE200	5' AT CAC AGA TCT CTC ACC ATG AGG CTC CCT GCT CAG 3'	2
	~~(SEQ ID NO: 6)~~ (SEQ ID NO: 10)	
GE202	5' AT CAC AGA TCT CTC ACC ATG GAA (A/G)CC CCA GC(T/G) CAG 3'	3
	~~(SEQ ID NO: 7)~~ (SEQ ID NO: 11)	
GE203	5' AT CAC AGA TCT CTC ACC ATG GTG TTG CAG ACC CAG GTC 3'	4
	~~(SEQ ID NO: 8)~~ (SEQ ID NO: 12)	

Light chain Vk-3' primer (BsiW I)

	113 112 111 110 109 108 107 106 105 104 103	
GE204	5' GG TGC AGC CAC CGT AGC TTT GAT (C/T)TC CA(G/C) CTT 3'	
	~~(SEQ ID NO: 9)~~ (SEQ ID NO: 13)	

Table 2

Primers for PCR of the lambda light chain variable domain of 6G5

NAME	Light chain Vl -early leader 5' (Bgl II)	FAMILY
	-20 -19 -18 -17 -16 -15	
744	5' AT CAC AGA TCT CTC ACC ATG (G/A)CC TG(G/C) TCC CCT CT 3'	1
	~~(SEQ ID NO: 10)~~ (SEQ ID NO: 14)	
745	5' AT CAC AGA TCT CTC ACC ATG GCC TGG (A/G)CT C(T/C)G CT 3'	2

~~(SEQ ID NO: 11)~~ (SEQ ID NO: 15)

910 5' AT CAC AGA TCT CTC ACC ATG GC(A/C) TGG A(T/C)C CCT CTC 3' 3
~~(SEQ ID NO: 12)~~ (SEQ ID NO: 16)

Light chain V1-3' primer (Avr II)

110 109 108 107 106 105 104

926 5' (AC)10 CTT GGG CTG ACC TAG GAC GGT 3' ~~(SEQ ID NO: 13)~~ (SEQ ID NO: 17)

Table 3

Primers for PCR of the heavy chain variable domains from 6G5 and 5E8

NAME	Heavy chain-early leaders 5' (Sal I)	Family
	-20 -19 -18 -17 -16 -15	
MB1503	5' GCG ACT AAG TCG ACC ATG GAC TGG ACC TGG 3'	1
~~SEQ ID NO: 14)~~	(SEQ ID NO: 18)	
MB1502	5' GCG ACT AAG TCG ACC ATG AAA CAC CTG TGG 3'	2,4
~~(SEQ ID NO: 15)~~	(SEQ ID NO: 19)	
GE207	5' GCG ACT AAG TCG ACC ATG GAG TTT GGG CTG AGC 3'	3
~~(SEQ ID NO: 16)~~	(SEQ ID NO: 20)	
GE208	5' GCG ACT AAG TCG ACC ATG GGG TCA ACC GCC ATC 3'	5
~~(SEQ ID NO: 17)~~	(SEQ ID NO: 21)	
GE209	5' GCG ACT AAG TCG ACC ATG TCT GTC TCC TTC CTC 3'	6
~~(SEQ ID NO. 18)~~	(SEQ ID NO: 22)	

Heavy chain-3' primer (Nhe I)

120 119 118 117 116 115 114 113 112 111 110

GE244 5' GC CAG GGG GAA GAC CGA TGG GCC CTT GGT GCT AGC TGA GGA GAC GG 3'
~~SEQ ID NO: 19)~~ (SEQ ID NO: 23)

GE210 5' GA TGG GCC CTT GGT GCT AGC TGA GGA GAC GG 3'
~~(SEQ ID NO: 20)~~ (SEQ ID NO: 24)

MB1533 5' GGT GCT AGC TGA GGA GAC GGT

109 108 107 106 105 104 103 101 100 99

GAC CAG GAC TCC CTG GCC CCA GAA GCC TAG 3'

~~(SEQ ID NO: 21)~~ (SEQ ID NO: 25)

Table 4

Sequencing Primers

Sp6 primer 5' AT TTA GGT GAC ACT ATA 3' ~~(SEQ ID NO: 22)~~ (SEQ ID NO: 26)

M13(-40)Forward Primer 5' GTT TTC CCA GTC ACG A 3' ~~(SEQ ID NO: 23)~~ (SEQ ID NO: 27)

T7 Promoter Primer 5' AT ATA CGA CTC ACT ATA GGG 3' ~~(SEQ ID NO: 24)~~ (SEQ ID NO: 28)

GE 108 Primer 5' CCG TCA GAT CGC CTG GAG ACG CCA 3' ~~(SEQ ID NO: 25)~~ (SEQ ID NO: 29)

377 Primer 5' GCA GTT CCA GAT TTC AAC TG 3' ~~(SEQ ID NO: 26)~~ (SEQ ID NO: 30)

607 PRIMER 5' CCA GGC CAC TGT CAC GGC TTC 3' ~~(SEQ ID NO: 27)~~ (SEQ ID NO: 31)

266 PRIMER 5' CAG AGC TGG GTA CGT CCT CA 3' ~~(SEQ ID NO: 28)~~ (SEQ ID NO: 32)

268 PRIMER 5' GCC CCC AGA GGT GCT CTT GG 3' ~~(SEQ ID NO: 29)~~ (SEQ ID NO: 33)

876 PRIMER 5' ACA CAG ACC CGT CGA CAT GG 3' ~~(SEQ ID NO: 30)~~ (SEQ ID NO: 34)

928 PRIMER 5' GCT CTC GGA GGT GCT CCT GG 3' ~~(SEQ ID NO: 31)~~ (SEQ ID NO: 35)

Table 5

PCR Primers Used for the Generation of a Glycosylation Mutantof the Heavy Chain Variable Region of 5E8

Sal I -20 -19 -18 -17 -16

MB 1650 5' ACA GAC CCG TCG ACC ATG GAG TTT GGG CTG 3' ~~(SEQ ID NO: 32)~~ (SEQ ID NO: 36)

Nhe I

118 117 116 115 114 113 112 111 110

MB 1651 5' CCC CTT GGT GCT AGC TGA GGA GAC GGT 3' ~~(SEQ ID NO: 33)~~ (SEQ ID NO: 37)

71 72 73 74 75 76 77 78 79

MB 1653 5' AGA GAG AAC GCC AAG AAC ACA CTG TTT 3' ~~(SEQ ID NO: 34)~~ (SEQ ID NO: 38)

79 78 77 76 75 74 73 72 71

MB 1654 5' AAA CAG TGT GTT CTT GGC GTT CTC TCT 3' ~~(SEQ ID NO: 35)~~ (SEQ ID NO: 39)

Please delete the sequence listing beginning at page 89 of the specification (in its entirety), which was amend on July 25, 2000, to include the sequence listing filed on that day, and in place thereof insert the sequence listing submitted herewith.

Amendments To The Claims

1-41. (Canceled)

42. (Currently amended) A chimeric anti-human CD23 antibody wherein the light chain variable domain consists of the ~~variable domain~~ polypeptide encoded by nucleotides 58-390 of SEQ ID NO: 1, the heavy chain variable domain consists of the ~~variable domain~~ polypeptide encoded by ~~SEQ ID NO: 2~~ nucleotides 48-423 of SEQ ID NO:3, and the constant region is a human constant region selected from the group consisting of human gamma-1 and human gamma-3 constant regions.

43. (Previously presented) The anti-human CD23 antibody of claim 42 wherein the human constant region is a human gamma-1 constant region.

44. (Previously presented) The anti-human CD23 antibody of claim 42 wherein the human constant region is a human gamma-3 constant region.

45. (Currently amended) A composition containing ~~an~~ the anti-human CD23 antibody according to claim 42 and a pharmaceutically acceptable carrier.

46. (Currently amended) A composition containing ~~an~~ the anti-human CD23 antibody according to claim 43 and a pharmaceutically acceptable carrier.

47. (Currently amended) A composition containing ~~an~~ the anti-human CD23 antibody according to claim 44 and a pharmaceutically acceptable carrier.

48. (Currently amended) A chimeric anti-human CD23 antibody wherein the light chain variable domain consists of the ~~variable domain~~ polypeptide encoded by ~~SEQ ID NO: 3~~ nucleotides 67-387 of SEQ ID NO: 5, the heavy chain variable domain consists of the ~~variable domain~~ polypeptide encoded by nucleotides 58-411 of ~~SEQ ID NO: 4~~ nucleotides 58-411 of SEQ ID NO: 7, and the constant region is a human constant region selected from the group consisting of a human gamma-1 constant region and a human gamma-3 constant region.

49. (Currently amended) A chimeric anti-human CD23 antibody wherein the light chain variable domain consists of the ~~variable domain~~ polypeptide encoded by ~~SEQ ID NO: 3~~ nucleotides 67-387 of SEQ ID NO: 5 and the heavy chain variable domain consists of the ~~variable domain~~ polypeptide encoded by ~~SEQ ID NO: 4~~ nucleotides 58-411 of SEQ ID NO: 7 with the exception that the asparagine codon encoded by nucleotides 289-291 of ~~SEQ ID NO:~~ 4 SEQ ID NO:7 is replaced with a lysine codon.

50. (Currently amended) The anti-human CD23 antibody according to claim 48 ~~which comprises~~ wherein the human constant region is a human gamma-1 constant region.

51. (Currently amended) The anti-human CD23 antibody according to claim 48 ~~which comprises~~ wherein the human constant region is a human gamma-3 constant region.

52. (Currently amended) The anti-human CD23 antibody according to claim 49 ~~which comprises~~ wherein the human constant region is gamma-1 constant region.

53. (Previously presented) The anti-human CD23 antibody according to claim 49 which comprises a human gamma-3 constant region.

54. (Currently amended) A composition comprising ~~an~~ the anti-human CD23 antibody according to claim 48 and a pharmaceutically acceptable carrier.

55. (Currently amended) A composition comprising ~~an~~ the anti-human CD23 antibody according to claim 49 and a pharmaceutically acceptable carrier.

56. (Currently amended) A composition comprising ~~an~~ the anti-human CD23 antibody according to claim 50 and a pharmaceutically acceptable carrier.

57. (Currently amended) A composition comprising ~~an~~ the anti-human CD23 antibody according to claim 51 and a pharmaceutically acceptable carrier.

58. (Currently amended) A composition comprising ~~an~~ the anti-human CD23 antibody according to claim 52 and a pharmaceutically acceptable carrier.

59. (Currently amended) A composition comprising ~~an~~ the anti-human CD23 antibody according to claim 53 and a pharmaceutically acceptable carrier.

60. (Canceled)

61. (Previously presented) The composition of claim 45, which composition is a pharmaceutical composition.

62. (Previously presented) The composition of claim 46, which composition is a pharmaceutical composition.

63. (Previously presented) The composition of claim 47, which composition is a pharmaceutical composition.

64. (Previously presented) The composition of claim 54, which composition is a pharmaceutical composition.

65. (Previously presented) The composition of claim 55, which composition is a pharmaceutical composition.

66. (Previously presented) The composition of claim 56, which composition is a pharmaceutical composition.

67. (Previously presented) The composition of claim 57, which composition is a pharmaceutical composition.

68. (Previously presented) The composition of claim 58, which composition is a pharmaceutical composition.

69. (Previously presented) The composition of claim 59, which composition is a pharmaceutical composition.

70-73. (Canceled)

Issue Classification	Application No.	Applicant(s)	
	09/019,441	REFF ET AL.	
	Examiner	Art Unit	
	Phuong Huynh	1644	

ISSUE CLASSIFICATION

ORIGINAL CLASS	ORIGINAL SUBCLASS	CLASS	CROSS REFERENCE(S) SUBCLASS (ONE SUBCLASS PER BLOCK)						
424	133.1	424	143.1						
INTERNATIONAL CLASSIFICATION		530	387.3	388.22					
A 61K	39/395								
C 12P	21/08								
C 07K	16/28								
	/								
	/								

Phuong Huynh 6/28/04
(Assistant Examiner) (Date)

(Legal Instruments Examiner) (Date) 7/2/4

Christina Chan
CHRISTINA CHAN
SUPERVISORY PATENT EXAMINER
(Primary Examiner) (Date)
TECHNOLOGY CENTER 1600 6/30/04

Total Claims Allowed: 27

O.G. Print Claim(s)	O.G. Print Fig.
1	None

☒ Claims renumbered in the same order as presented by applicant ☐ CPA ☒ T.D. ☐ R.1.47

Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original
	1		31	19	61		91		121		151		181
	2		32	20	62		92		122		152		182
	3		33	21	63		93		123		153		183
	4		34	22	64		94		124		154		184
	5		35	23	65		95		125		155		185
	6		36	24	66		96		126		156		186
	7		37	25	67		97		127		157		187
	8		38	26	68		98		128		158		188
	9		39	27	69		99		129		159		189
	10		40		70		100		130		160		190
	11		41		71		101		131		161		191
	12	1	42		72		102		132		162		192
	13	2	43		73		103		133		163		193
	14	3	44		74		104		134		164		194
	15	4	45		75		105		135		165		195
	16	5	46		76		106		136		166		196
	17	6	47		77		107		137		167		197
	18	7	48		78		108		138		168		198
	19	8	49		79		109		139		169		199
	20	9	50		80		110		140		170		200
	21	10	51		81		111		141		171		201
	22	11	52		82		112		142		172		202
	23	12	53		83		113		143		173		203
	24	13	54		84		114		144		174		204
	25	14	55		85		115		145		175		205
	26	15	56		86		116		146		176		206
	27	16	57		87		117		147		177		207
	28	17	58		88		118		148		178		208
	29	18	59		89		119		149		179		209
	30		60		90		120		150		180		210

12. The chimeric anti-human CD23 antibody according to claim 8 which comprises a human gamma-3 constant region.

13. A composition comprising the chimeric anti-human CD23 antibody according to claim 8 and a pharmaceutically acceptable carrier.

14. A composition comprising the chimeric anti-human CD23 antibody according to claim 8 and a pharmaceutically acceptable carrier.

15. A composition comprising the chimeric anti-human CD23 antibody according to claim 9 and a pharmaceutically acceptable carrier.

16. A composition comprising the chimeric anti-human CD23 antibody according to claim 10 and a pharmaceutically acceptable carrier.

17. A composition comprising the chimeric anti-human CD23 antibody according to claim 11 and a pharmaceutically acceptable carrier.

18. A composition comprising the chimeric anti-human CD23 antibody according to claim 12 and a pharmaceutically acceptable carrier.

19. The composition of claim 4, which composition is a pharmaceutical composition.

20. The composition of claim 5, which composition is a pharmaceutical composition.

21. The composition of claim 6, which composition is a pharmaceutical composition.

22. The composition of claim 13, which composition is a pharmaceutical composition.

23. The composition of claim 14, which composition is a pharmaceutical composition.

24. The composition of claim 15, which composition is a pharmaceutical composition.

25. The composition of claim 16, which composition is a pharmaceutical composition.

26. The composition of claim 17, which composition is a pharmaceutical composition.

27. The composition of claim 18, which composition is pharmaceutical composition.

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